REMARKS

I. Status of the Claims

Claims 1-54 were originally filed. Claims 1-30, 34-48, and 52-54 were withdrawn from consideration due to a restriction requirement. Claims 55-74 were later added.

Upon entry of the present amendment, claims 31-33 as well as all withdrawn claims are canceled. Claims 49, 55, and 56 are amended to recite specific hybridization conditions, which are found in the specification, *e.g.*, on page 20, lines 28-31, and page 21, lines 2-4. Claims 49, 55, and 57 are also amended to recite that one or both of the T1R3 and T1R2 polypeptides are recombinant, support for which is found throughout the specification, particularly in the examples and in original claim 34. Claims 49 and 55 are further amended to recite that the sweet taste receptor specifically binds a sweet compound, which is supported by the specification, *e.g.*, on page 32 lines 27-30 and page 57 lines 9-27. Claim 57 is amended to correct a typographic error by replacing "SEQ ID NO:6, 7, or 8" with "SEQ ID NO:7, 8, or 9," which is supported by claim 55. Claim 64 is amended to replace "the" with "an," according to the Examiner's suggestion. Claim 65 is further amended to replace "expressed" with "present" to clarify the meaning of the claim language.

New claims 75 and 78 are drawn to methods of identifying a compound that modulates sweet taste signal transduction using a sweet taste receptor comprising a T1R1 polypeptide and a T1R3 polypeptide, support for which is found in the specification and claims 49 and 55. No new matter is introduced due to the present amendment.

Claims 49-51, 55-74, and 75-78 are currently under examination.

II. Objections to Drawings

The drawings were objected to. A set of corrected drawings is filed concurrently with this response.

III. Objections to Specification

A. Priority

The Examiner objected to the reference on page 1, lines 6-9, of the present application to several U.S. patent applications (USSN 60/095,464; 60/112,747; 09/361,631; 60/094,465; and 09/361,652) as "related applications," and required clarification as to whether Applicants intend to claim priority to these applications. Applicants do not intend to claim priority to these applications and have amended the specification accordingly.

B. Hyperlink

The Examiner also objected to the specification for an embedded hyperlink. The specification has been amended to delete the hyperlink.

IV. Claim Objections

Claims 31-33 were objected to for being dependent from a non-elected base claim. The present amendment has addressed this issue.

V. Claim Rejections

A. 35 U.S.C. §112, Second Paragraph

Claims 31-33, 49-51, and 55-74 were rejected under 35 U.S.C. §112, second paragraph, for alleged indefiniteness. Applicants hereby address the rejections in the order the Examiner presented them.

"Modulators"

The Examiner asserted that the specification has not set forth the meaning the term "modulator" may have other than "activator" or "inhibitor." Applicants respectfully traverse the assertion.

The definition of "modulator" is given on page 13, line 26, to page 14, line 24. The same section also contains a general description of assay methods to determine if a compound is a "modulator." The section from page 14, line 25, to page15, line5, provides additional description of the nature and properties of a "modulator." Furthermore, on page 10,

lines 19-22, of the present application, it is stated that modulators may include "activators, inhibitors, stimulators, enhancers, agonists, and antagonists." These terms have meanings different from each other, although some are similar and may overlap in scope to varying degrees. Applicants submit that, based on the present disclosure, a person skilled in the art would readily recognize the metes and bounds of the term "modulator" and would therefore not found the term ambiguous.

"Moderately Stringent Conditions"

The Examiner held that the recitation of "moderately stringent conditions" is indefinite. In response, Applicants have amended relevant claims to recite specific conditions for both "highly stringent" and "moderately stringent" hybridization conditions.

Antecedent Basis for "the T1R2 Polypeptide" and "Heterologous Polypeptide"

The Examiner pointed to the lack of antecedent basis for "the T1R2 polypeptide" in claim 33 and for "heterologous polypeptide" in claims 31 and 32. This point is moot as claims 31-33 are now canceled.

"Functional Effect"

The Examiner alleged that the term "functional effect" as recited in claims 55-74 is ambiguous. Applicants do not agree. The definition for this term is provided on page 13, lines 1-7, where it states,

> The phrase "functional effects" in the context of assays for testing compounds that modulate activity (e.g., signal transduction) of a sweet taste receptor or protein of the invention includes the determination of a parameter that is indirectly or directly under the influence of a GPCR or sweet taste receptor, e.g., a physical, phenotypic, or chemical effect, such as the ability to transduce a cellular signal in response to external stimuli such as ligand binding, or the ability to bind a ligand. It includes binding activity and signal transduction. "Functional effects" include *in vitro*, *in vivo*, and *ex vivo* activities.

By way of giving examples, this description sufficiently allows one of skill in the art to ascertain which assay activities are encompassed by the step of "determining functional

effects" as recited in the pending claims, see page 13, lines 8-25. These detailed descriptions allow an ordinarily skilled artisan to determine the metes and bounds of term "functional effect." Applicants hence submit that the term is not indefinite.

"The Extracellular Domain"

The Examiner asserted that the term "the extracellular domain" in claim 64 is ambiguous and suggested that the term be replaced with "an extracellular domain." Claim 64 has been amended as such. Applicants thank the Examiner for the helpful suggestion.

"Expressed in a Cell or Cell Membrane"

The Examiner asserted that the term "expressed in a cell or cell membrane" as recited in claims 65 and its dependent claims has unclear meanings. This phrase has been replaced with "present in a cell or cell membrane" in claim 65 upon entry of the present amendment.

B. 35 U.S.C. §112, First Paragraph

Claims 31-33, 49-51, and 55-74 were rejected under 35 U.S.C. §112, first paragraph, for alleged lack of proper enablement. Applicants respectfully traverse the rejection in light of the present amendment. The Examiner's specific concerns will be addressed below in the order in which they were raised.

According to the MPEP, to satisfy the enablement requirement, the information contained in a patent specification must be sufficient to inform one skilled in the relevant art how to both make and use the claimed invention. MPEP §2164. Whether the enablement requirement is met depends on whether undue experimentation is necessary for one of skill in the art to practice the invention in light of the disclosure. MPEP §2164.01.

The pending claims are drawn to methods for identifying modulators of sweet taste signal transduction, using a sweet receptor as a reporter of altered signal transduction. As amended, the pending claims recite that the sweet receptor, a T1R3/T1R2 heterodimer, specifically binds a sweet compound.

a. T1R2 or T1R3 Variants

In the Office Action mailed August 26, 2003, the Examiner asserted that the specification does not enable the claimed methods for identifying modulators for sweet taste signal transduction using a heterodimer sweet receptor comprising T1R3 and T1R2 variants, because the specification gives no guidance as to how to make these variants having sequences different from SEQ ID NO:9 and SEQ ID NO:15, and because it is unclear what desired properties these T1R3 and T1R2 variants should retain. The Examiner further stated that the specification has not provided any working example of artificially constructed variants based on SEQ ID NOs:9 and 15.

Applicants submit that the newly added recitation, *i.e.*, the sweet receptor specifically binds a sweet compound, sufficiently sets forth the commonly shared functional feature of the sweet receptors used in the claimed methods. There should be no dispute that given the level of technical sophistication in the field of molecular biology, sequence variants of SEQ ID NO:9 or 15 can be easily made. Relying on the commonly shared functional feature, one of skill in the art can readily screen for variants that retain such functionality and are therefore suitable for practicing the claimed invention. This screening process relies on routine techniques in protein chemistry that are often employed by a skilled artisan. The specification further provides guidance on how to detect the specific binding of a sweet taste receptor to a sweet compound (*see, e.g.*, page 32 lines 17-35). Thus, Applicants contend that any experimentation necessary for determining which variants would be useful for practicing the claimed invention is merely routine and does not constitute undue experimentation.

In response to the Examiner's assertion that there is no working example of a T1R2 or T1R3 variant, Applicants submit that the existence of a working example is merely one of many factors to be considered for determining whether any particular experimentation is undue, according to the Federal Circuit in *in re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The lack of working examples alone does not necessary support the conclusion of undue experimentation and failure to enable. MPEP §2164.02. In the present case, the specification does provide working examples within the scope of the claimed invention, namely, SEQ ID

NO:9 and SEQ ID NO:15. The lack of a working example of a T1R2 or T1R3 variant thus carries only limited weight, particularly in light of the high level of skill in the art and routine nature of the techniques for making these variants.

b. Identifying Modulators when Receptor Is Not Present on Cell Membrane

The Examiner also stated that the claimed invention is not enabled because in the cases where the sweet receptor is not present in the cell membrane, the specification does not provide guidance as to what methods can be used to detect the receptor's response to a ligand.

Applicants disagree with the Examiner. The specification does offer various methods that can be used for detecting sweet taste signal transduction, including methods useful in a cell-free context (*see, e.g.*, page 31, lines 21-31), such as protein-protein binding assays, gel mobility shift assays, immunoassays, and enzymatic assays in a competitive or noncompetitive format (*see, e.g.*, page 32, lines 17-34). For example, the specification teaches measuring sweet taste signal transduction based on ligand binding, which is certainly suitable for practice in a cell-free assay system, such as the case where a sweet taste receptor is immobilized to a solid support.

c. G-Proteins

The Examiner further alleged that the claimed invention is not fully enabled because the claims encompass the use of a sweet receptor coupled with an endogenous G-protein, yet the specification does not provide any G-proteins useful for the present invention besides Gα15, nor are such additional G-proteins known in the art.

The omission to name additional G-proteins that may be used in connection with a sweet receptor to practice the present invention does not constitute sufficient ground for an enablement rejection. The pending claims recite the use of a sweet receptor comprising a T1R3/T1R2 heterodimer for identification of modulators of sweet taste signal transduction. G-proteins are merely one type of additional components that can be possibly used in connection with the heterodimer sweet receptor in practicing the claimed method. Theoretically unlimited number of other components may be further used in addition to the sweet receptor. It would be

an impossible task if a patent applicant had to name and describe all potential additional components in order to the satisfy the enablement requirement for claims reciting an open transitional phrase.

Moreover, there are other G-proteins known in the art that may be useful in the present invention. Examples of these G-proteins include: α-gustducin, Gα14, and Gα16 (*see, e.g.*, page 57, lines 3-6, of the specification and Nelson *et al.*, IDS reference C6).

Applicants thus contend that the enablement rejection based on lack of description of G-proteins is improper and respectfully request its withdrawal.

d. Modulator v. Activator or Inhibitor

Additionally, the Examiner took the position that the claimed invention is not enabled because the claimed methods are for identifying "modulators" of sweet taste signal transduction, whereas the specification teaches only the identification of activators or inhibitors.

Applicants dispute the Examiner's characterization of the teaching of the instant specification. Instead of teaching how to identify only the activators or inhibitors, Applicants contend that the instant disclosure teaches the identification of any compound that is capable of affecting the signal transduction of a T1R3/T1R2 heterodimer sweet receptor in any manner, which encompasses activation, inhibition, and other types of modulation. This is because such a modulator, as long as it alters the patterns of signal transduction in sweet perception by a T1R3/T1R2 heterodimer sweet receptor, will be detected using the assay systems taught by the present application, such as those described on page 32 line 1 to page 36 line 15, and those exemplified in Figures 5-6 and on page 8 line 20 to page 9 line 21.

In summary, no undue experimentation would be necessary to practice the invention as claimed. Accordingly, Applicants respectfully request that the enablement rejection under 35 U.S.C. §112 be withdrawn.

C. 35 U.S.C. §102

Claims 31-33, 49, 50, 55-57, 59, 65, 71-73 were rejected under 35 U.S.C. §102(b) for alleged anticipation by Kinnamon *et al.* Applicants respectfully traverse the rejection in light of the present amendment.

To anticipate a pending claim, a prior art reference must contain all limitations of the claim. MPEP §2131. As amended, the pending claims are directed to methods for identifying compounds that can modulate sweet taste signal transduction in taste cells using a sweet taste receptor comprising T1R3 and T1R2 polypeptides, of which at least one is recombinant.

In contrast, the Kinnamon reference relates to studies of taste signal transduction mediated by naturally occurring taste receptors in taste cells. No taste receptor comprising any recombinant polypeptide is involved in the studies. This reference thus does not provide all limitations of the pending claims. In fact, the present inventors were the first to describe the sweet taste receptor comprising T1R3 and T1R2 subunits.

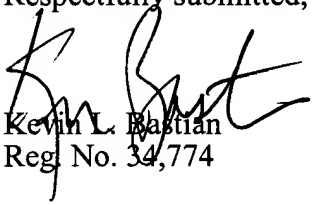
As such, Applicants respectfully request that the anticipation rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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